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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/647,069	09/26/2000	Laure Boymond	48937	3836

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KEIL & WEINKAUF
1350 CONNECTICUT AVENUE, N.W.
WASHINGTON, DC 20036

EXAMINER

EPPERSON, JON D

ART UNIT	PAPER NUMBER
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1639

DATE MAILED: 03/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary*File Copy*

Application No.

09/647,069

Applicant(s)

BOYMOND ET AL.

Examiner

Jon D Epperson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 December 2002.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

Please note: The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1639.

Status of the Application

1. The Response and Amendment filed December 19, 2002 (Paper No. 11) is acknowledged. Furthermore, the Supplemental Response filed January 3, 2003 is also acknowledged (see Paper No. 12).
2. The text of those sections of Title 35, U.S. code not included in this action can be found in a prior Office action.

Status of the Claims

3. Claims 1-5 were pending. Claim 1 was amended and claim 5 was cancelled. Therefore, claims 1-4 are pending.

Election/Restriction

4. This application contains claims 6-8 drawn to inventions nonelected in Paper No. 6. This was addressed in the previous action. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

Withdrawn Objections/Rejections

5. The rejections under 35 U.S.C. 112, second paragraph, denoted "A" and "B" in the previous office are withdrawn in view of applicant's amendments to the claims and/or arguments. The rejection under 35 U.S.C. 102(a) is withdrawn in view of applicant's arguments and in view of applicant's submission of a foreign priority English translation. The rejection under 35 U.S.C. 102(b) is also withdrawn in view of applicant's amendments and/or arguments. All other rejections are maintained and the arguments are addressed below.

Outstanding Objections and/or Rejections

35 USC § 103

6. Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ohno et al (US 5420310) (Date of Patent is **May 30, 1995**) in view of Minoura et al (*J. Polym. Sci., Part A-1*, 1969, 7(11), 3245-55) and Capporiccio et al (US 4,254,030) (Date of Patent is **March 3, 1981**).

Ohno teaches the same magnesium-halogen exchange reaction disclosed by the applicant, which reads on claims 1-4 (see ***Claim Rejections - 35 USC § 102*** in Paper No. 10, incorporated in its entirety herein by reference). However, Ohno lacks the teaching of carrying out the magnesium-halogen exchange reaction on a solid support as recited in the currently amended claims.

However, Minoura *et al* (*J. Polym. Sci., Part A-1*, 1969, 7(11), 3245-55) teaches the synthetic usefulness of performing a magnesium-halogen exchange reaction on a

solid support using poly(vinyl chloride) as the solid support and benzylmagnesium chloride as the compound of general formula III (see Minoura et al, page 3249, reaction 5). Caproiccio et al also teaches the synthetic usefulness of performing a magnesium-halogen exchange reaction on a solid support using copolymers of fluorosulphonyl olefins (see Caproiccio et al, column 3, reaction V).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art to carry out the magnesium-halogen exchange reaction described by Ohno et al on a solid support, as taught by Minoura *et al*. One would have been motivated to use a magnesium-halogen exchange reaction on a solid support to obtain higher yields that are “free of by-products, avoiding any interaction between ... [functionalities that are labile to Grignard reagents] and Grignard compounds, [and] ... also avoiding secondary reactions between the different species present during the course of the reaction” (see Caproiccio et al, column 8, lines 22-29). One would have had a high expectation of success since both Minoura et al and Caproiccio et al teach that magnesium-halogen exchange reactions can occur for reactions involving alkyl halides on a solid support.

Response to Arguments

7. Applicant's arguments have been fully considered but they are not found persuasive. The Examiner's rationale is set forth below.

Applicant argues, “The examiner has failed to establish a *prima facie* case of obviousness. The references cited by the examiner do not provide a suggestion or motivation to combine the teachings to produce the instant invention. As noted above, the examiner suggests

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that one of ordinary skill in the art would have been motivated to produce the instant invention because Caporiccio suggests that higher yields may be obtained. However, this citation that higher yield may be obtained refers to a process that does not produce compound of formula I, nor does it involve compounds of the formula II" (see Paper 11, page 7, paragraph 1).

The Examiner's position is that the motivation provided in the 35 USC §103(a) rejection above is proper. The Caporiccio et al reference does not have to teach applicant's cited compounds because if it did it would be a 35 USC §102(b) rejection, not a 35 USC 103(a) rejection i.e., the reference does not have to teach every limitation in applicants claimed invention e.g., applicants cannot argue the Caporiccio et al reference "alone" does not teach every limitation of applicant's claimed invention. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

The Caporiccio et al reference only has to provide a motivation to combine the references together. In this regard, the Examiner argued in the previous action that:

One would have been motivated to use a magnesium-halogen exchange reaction on a solid support to obtain higher yields that are "free of by-products, avoiding any interaction between ... [functionalities that are labile to Grignard reagents] and Grignard compounds, [and] ... also avoiding secondary reactions between the different species present during the course of the reaction" (see Caporiccio et al, column 8, lines 22-29).

Consequently, a motivation to synthesize the compounds of Ohno et al on solid-phase as taught by Caporiccio et al [and Minoura et al] was properly cited (i.e., a motivation to obtain cleaner products and better yields). This motivation for cleaner products and higher yields was

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well known to those of skill in the art at the time of filing for performing any solution based organic chemistry reaction on a solid-support (i.e., a person of skill in the art would always have been motivated to perform any solution based organic reaction on a solid-support to increase purity and yield). However, in the interests of providing a specific reference that teaches this motivation not only for organic chemistry reactions in general, but more specifically to teach applicant's claimed Grignard reactions, the Examiner has gone one step further and provided "two" specific examples (i.e., Caporiccio et al and Minoura et al) wherein persons of skill in the art were motivated to obtain higher yields and higher purity by performing applicant's claimed Grignard reactions (i.e., the cited references and applicant's claimed invention possess the exact same mechanism of action for the magnesium-halogen exchange). Therefore, the motivation to obtain cleaner products in higher yields by using solid-phase synthesis instead of solution-phase synthesis (i.e., that are "free of by-products" while "avoiding secondary reactions" that would result in lower yields, see 35 USC §103(a) rejection above) is entirely applicable to all solid-phase reactions and especially to applicant's claimed invention because applicant's Grignard reactions were specifically cited by the "two" exemplary references provided by the Examiner and thus would more specifically point to applicant's claimed invention than a general teaching about the usefulness of solid-phase synthesis that did not specifically recite the use of Grignard reagents.

Applicant further argues, "Furthermore, a single line in a reference should not be taken out of context and relied upon with the benefit of hindsight to show obviousness. *Baush & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.*, 796 F.2d 443, 230 USPQ 416 (Fed. Cir. 1986). Thus, the examiner seems to suggest that it would have been "obvious to try" the process of the

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instant invention as a result of the references cited. However, this is not the standard of invention under 35 USC §103. "Obvious to try" is not a valid test of patentability. In re Dow Chemical company, 5 USPQ2d 1529, 1532 (Fed. Cir. 1998).

The Examiner's position here is that the above 35 USC §103 rejection has not used references "out of context" as suggest by applicant not applied an "obvious to try" test. Here, applicants have stated that the Examiner cited the references "out of context", but applicants have not provided any basis (i.e., no scientific reasoning) for making such a statement. Furthermore, applicants have not shown what "alternative" context they believe these references are made under. Consequently, it is the Examiner's position that applicant's unsubstantiated statements are not persuasive. Furthermore, the Examiner has never put forth an "obvious to try" standard anywhere in the 35 USC §103 rejection above. The Examiner has specifically stated the motivation for combining the references (i.e., higher yields and purity, see quotation above) and, as a result, applicant's unsubstantiated statements are again not persuasive.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Applicant further argues, "Second, the examiner has failed to show that the applicants had an expectation of success. The examiner argues that applicants had an expectation of

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success of the claimed invention as “both Minoura et al and Caproiccio et al teach that magnesium-halogen exchange reactions can occur for reaction involving alkyl halides on solid support.” (Paper number 10, page 9). However, these references do not suggest the success of the instant invention as they pertain to processes utilizing poly vinyl chloride (Minoura) and fluorosulphonyl olefins (Capoiccio). However, neither of these process utilize the compound of the formula I in the instant invention and therefore these references do not suggest the success of the instant invention.”

First, the Examiner’s position is that applicant’s statement that the references “do not suggest the success of the instant invention as they pertain to processes utilizing poly vinyl chloride (Minoura) and fluorosulphonyl olefins (Capoiccio)” is not applicable to the currently pending claims because they do not specify the solid support in the claims. In response to applicant's argument that the references fail to show certain features of applicant’s invention, it is noted that the features upon which applicant relies (i.e., the type of polymer employed in the solid-phase reaction) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).”

Second, the Examiner has stated in the previous office action a reason that one of skill in the art would expect to be successful:

One would have had a high expectation of success since both Minoura et al and Caproiccio et al teach that magnesium-halogen exchange reactions can occur for reactions involving alkyl halides on a solid support

(see 35 USC §103(a) rejection above). The reactions as taught by Minoura et al and Caproiccio et al both employ Grignard reagents on solid-phase that operate under the exact same

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“mechanism” as those disclosed by applicants i.e., magnesium-halogen exchange. The Grignard reactions have been known since the early 1900’s and the mechanism of reaction is well established (the reaction is published in almost every undergraduate organic chemistry text book) and, as a result, there is no reason set forth by applicants or the literature that would indicate that the reaction is “unpredictable” and wouldn’t work for the compounds disclosed by Ohno et al in view of the teachings of Caproiccio et al and Minoura et al. Thus, the Examiner has established that there would be “a high expectation of success.”

Finally, the Minoura et al and Caproiccio et al references do not have to teach “the compound of the formula I” because if they did they would be 35 USC §102(b) rejections, not 35 USC §103(a) rejections i.e., the reference does not have to teach every limitation in applicants claimed invention e.g., applicants cannot argue the Caporiccio et al reference “alone” does not teach every limitation of applicant’s claimed invention. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The Examiner has put forth specific reasons for a “reasonable expectation of success” as stated above.

Finally, applicant argues, “in effect the examiner has chosen to combine these three references with the hindsight of the applicants specification. However, one cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988). Therefore,

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applicants respectfully assert that a prima facie case of obviousness has not been established and request that the rejection be withdrawn.”

The Examiner's position is that “hindsight” was not used and that applicant's specification was never cited or relied upon in the manner suggested by applicants. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Accordingly for all the reasons stated above the rejection is maintained.

References Illustrative of the State of the Prior Art

- 1) Hermkens, P. H. H.; Ottenheijm, H. C. J.; Rees, D. “Solid-Phase Organic Reactions: A Review of the Recent Literature” *Tetrahedron*. **1996**, 52, 13, 4527-4554, see entire document, more particularly pages 4530-4548, most particularly page 4547 i.e., “Grignard” entry, showing general applicability of solid-phase chemistry to a broad range of solution-phase chemical reactions including the Grignard reaction.
- 2) Solomons, Graham T. W. Organic Chemistry 5th Edition. New York: John Wiley & Sons, Inc. 1992, pages 458-475, showing that the mechanism for Grignard reactions is established and well known in the art.

Conclusion

8. Applicant's amendment necessitated any new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D. Epperson, Ph.D. whose telephone number is (703) 308-2423. The examiner can normally be reached on Monday-Thursday from 9:30 to 7:00 and alternate Fridays.

10. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Any inquiry of

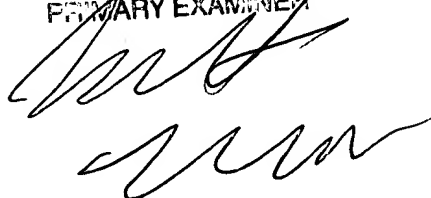
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a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Jon D. Epperson, Ph.D.

February 26, 2003

BENNETT CELSA
PRIMARY EXAMINER

A handwritten signature in black ink, appearing to read 'Bennett Celsa', is written over the printed name and title.